

*Application No. 10/649,457**Reply to Office Action***REMARKS/ARGUMENTS****BEST AVAILABLE COPY***Status of the Claims*

Claims 1-3, 6-21, and 42-57 are pending, with claims 11-12 withdrawn, and claims 4-5, and 22-41 canceled. Claims 42-57 are new. Claims 1-10, 13-21, and 42-57 are being actively prosecuted at this time and claims 11 and 12 are withdrawn. With respect to claims that have been withdrawn, upon allowance of the composition claims, Applicants may move for rejoinder of the withdrawn claims dependent thereon or which contain each limitation of the allowed claims. Claims 1-3 and 20 are amended herein and claims 42-57 are new. No new matter has been added by way of the claim amendments or the addition of claims.

Amendments to the Specification

The Office Action objects to paragraph [0071] for containing a hyperlink embedded therein. Paragraph [0071] has been amended to delete the hyperlink. Applicants request that the rejection be withdrawn.

Paragraphs [0004] and [0030] are amended to correct typographical errors.

Discussion of Section 112 Rejections

Claim 1-10 and 13-21 are rejected under 35 U.S.C. § 112 as allegedly indefinite for reciting the phrase "codons expressed more frequently in humans." Claim 1 has been amended and no longer recites this phrase. Therefore, Applicants respectfully request that the rejection be withdrawn.

Discussion of Section 103 Rejection

Claims 1-10 and 13-21 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the combination of Gu (*Vaccine*, 17: 340-344 (1999)), Wu (*Proc. Natl. Acad. Sci. USA*, 92: 11671-11675 (1995)), Farina (*J. Virol.*, 75(23): 11603-11613 (2001)), Mogridge (*J. Bacteriol.*, 183(6): 2111-2116 (2001)), and Hamdan (*Parasitol. Res.*, 88: 583-586 (2002)). Applicants traverse the rejection.

Applicants assert that one skilled in the art would not have been motivated to combined the *five* cited references in order to produce the invention. The only way in which

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the combined disclosures of the Gu, Wu, Farina, Mogridge, and Hamdan references can be considered as teaching or suggesting the present invention as defined by the claims (prior to amendment herein) is through the use of hindsight, i.e., with the knowledge of the present application and the invention as claimed therein. It is impermissible for the Patent Office to engage in hindsight reconstruction of the claimed invention by using Applicants' invention as a template and selecting and combining elements from references to fill in that template. See *In re Gorman*, 933 F.2d 982, 18 U.S.P.Q.2d 1885 (Fed. Cir. 1991).

Further, the claims, in their present form, recite that the nucleic acid comprises SEQ ID NO: 1, which is not taught or suggested by the cited references, alone or in combination. SEQ ID NO: 1 encodes protective antigen (PA), an exotoxin of *Bacillus anthracis*, which has been humanized (i.e., contains human preferred codons). None of the cited references teaches a humanized sequence encoding PA. Farina and Wu teach the production of a chimpanzee vector and a LAMP sorting signal, respectively. Neither reference discloses any sequences of *B. anthracis*. In order to determine the function of various domains of PA, Mogridge teaches a mutated amino acid sequence of PA that impairs oligomerization. Mogridge does not teach a DNA sequence encoding PA optimized for human expression. As SEQ ID NO: 1 encodes PA with human preferred codons, and not a mutated amino acid sequence, Mogridge is not instructive. Gu teaches a plasmid containing native DNA encoding PA. Gu does not teach the humanized DNA sequence of SEQ ID NO: 1. Hamdan discloses that preferred human codon usage may increase expression of *Schistosoma mansoni* cDNA and states that its methods may be used to optimize expression of any DNA from helminths or other parasites (see Abstract). Therefore, none of the cited references recites SEQ ID NO: 1, which is required by each pending claim.

It is well-settled, that in order to establish a *prima facie* case of obviousness with respect to a claim, at least two criteria must be met: (1) the prior art references must suggest to one of ordinary skill in the art to make the subject matter defined by the claims in issue and (2) the prior art references must provide one of ordinary skill in the art with a reasonable expectation of success in so making the subject matter defined by the claims in issue. Both the suggestion and the reasonable expectation of success must be found in the prior art references, not in the disclosure of the patent application in issue. See, e.g., *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). As discussed above, the first


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criteria is not met as the cited references fail to disclose or suggest SEQ ID NO: 1. Nor is the second criteria met, as one skilled in the art would not have a reasonable expectation of success utilizing the teachings found in the cited art. Hamdan is the only reference that discloses codon optimization, and it only teaches the rewriting of the first half of the cDNA sequence (which, in *S. mansoni*, contained the majority of nonhuman preferred codons). The authors state that to rewrite the entire cDNA sequence "would have complicated the recursive PCR further" (see page 586). In addition, the authors state that the mutagenic oligonucleotides had to be carefully checked to minimize hairpin formation which is common in longer primers as well as to avoid the introduction of cryptic splice sites that may produce truncated products (see page 584). If one skilled in the art were to use the teachings in Hamdan, one would have no guidance in rewriting an entire DNA sequence with human preferred codons, nor any instruction as to what technical issues may arise therefrom or how to solve them. One skilled in the art would not have a reasonable expectation of success in preparing a DNA sequence for PA containing human preferred codons using the teachings found in Hamdan. Therefore, the first and second criteria for establishing a prima facie case of obviousness have not been met. Applicants respectfully request that the rejection be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,


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